Postnatal depression: drug treatments

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ABSTRACT

INTRODUCTION: The differentiation between postnatal depression and other types of depression is often unclear, but there are treatment issues in nursing mothers that do not apply in other situations. The point prevalence of major depressive disorder in predominantly high-income countries is about 5% in the first 3 months postpartum. When minor depression is included, it increases to 13%, with a period prevalence rate of 19%. These figures increase further in low-income countries. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of drug treatments for postnatal depression? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 418 studies. After deduplication and removal of conference abstracts, 201 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 139 studies and the further review of 62 full publications. Of the 62 full articles evaluated, one systematic review was updated, and two systematic reviews and one RCT were added at this update. We performed a GRADE evaluation for three PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for four interventions based on information about the effectiveness and safety of SSRI antidepressants, antidepressants other than SSRIs, hormones, and St John's Wort.

QUESTIONS

INTERVENTIONS

DRUG TREATMENTS

Likely to be beneficial

Unknown effectiveness

Covered elsewhere in Clinical Evidence

Depression in adults: drug and other physical treatments.

Footnote

*Antidepressants are categorised on the evidence of their effectiveness in the treatment of depression in general.

Key points

- The differentiation between postnatal depression and other types of depression is often unclear, but there are treatment issues in nursing mothers that do not apply in other situations.

  The point prevalence of major depressive disorder in predominantly high-income countries is about 5% in the first 3 months postpartum. When minor depression is included, it increases to 13%, with a period prevalence rate of 19%. These figures increase further in low-income countries.

  Most episodes resolve spontaneously within 3 to 6 months, but 30% of depressed mothers still have symptoms at 1 year. Depression can interfere with the mother-infant relationship, which can significantly affect infant neurodevelopment.

  Suicide is a major cause of maternal mortality in resource-rich countries, but rates are lower in women postpartum than in women who have not had a baby.

- SSRIs may improve symptoms of postnatal depression, but we found few studies evaluating their effect specifically in postpartum women.

  We do not know whether other types of antidepressant are effective compared with placebo.

  We do not know whether oestrogen treatment or St John's Wort improve symptoms compared with placebo.

Clinical context

GENERAL BACKGROUND

A systematic review of studies from 1980 through March 2004 suggests that the point prevalence of major depressive disorder in predominantly high-income countries is about 5% in the first 3 months postpartum. When minor depression is included, it increases to 13%, with a period prevalence rate of 19%. These figures increase further in low-income countries. Although most women with postnatal depression recover within a few months, approximately 30% remain depressed after a year. The management of depression during this period is particularly important as it can have a significant impact on infant neurodevelopment. Furthermore, postnatal mental illness remains a leading cause of maternal mortality, although rates are lower in women postpartum than in women who have not had a baby.

FOCUS OF THE REVIEW

In the UK, there is an absence of marketing authorisation for any psychotropic medication to be taken by women who are breastfeeding. This leaves the prescriber fully responsible for providing up-to-date information, so the woman can make an informed decision. Therefore, while we acknowledge that there are effective non-drug treatments for postnatal depression, the focus of this overview will be on pharmacological treatments.

COMMENTS ON EVIDENCE

We found RCT evidence for two of our five interventions relative to placebo. No direct information from RCTs was found for fluoxetine versus placebo, paroxetine versus placebo, or St John's Wort versus placebo. One RCT reported no significant difference in the remission of depression following randomisation to sertraline and nortriptyline (a tricylic antidepressant). Despite the lack of good-quality evidence comparing SSRIs with placebo directly, SSRIs are likely to be beneficial for the treatment of postnatal depression based on evidence of their effectiveness in treating depressive disorders in general, and also in the treatment of premenstrual dysphoric disorder.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, May 2008, to March 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 418 studies. After deduplication and removal of conference abstracts, 201 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 139 studies and the further review of 62 full publications. Of the 62 full articles evaluated, one systematic review was updated, and two systematic reviews and one RCT were added at this update

DEFINITION

Postnatal depression (PND) has been variously defined as non-psychotic depression occurring during the first 6 months, the first 4 weeks, and the first 3 months postpartum. In the UK, 3 months postpartum has been suggested as a useful clinical definition. [1] Puerperal mental disorders have only in the last 20 years been categorised separately in psychiatric classifications. However, both the ICD-10 [2] and the DSM-5 (see table 1, p 9) require certain qualifications to be met that limit their use: ICD-10 categorises mental disorders that occur postpartum as puerperal, but only if they cannot otherwise be classified; and DSM-5 requires that patients must meet the criteria for a major depressive episode with an onset in pregnancy or within 4 weeks of delivery. [3] In clinical practice and research, the broader definition above is often used, because whether or not PND is truly distinct from depression in general, depression in the postpartum period raises treatment issues for the nursing mother and has implications for the developing infant (see Prognosis, below). Furthermore, there is increased recognition that the depression often starts during pregnancy (as reflected in the new DSM-5 criteria). [4] [5] The symptoms are similar to symptoms of depression at other times of life, but in addition to low mood, sleep disturbance, change in appetite, diurnal variation in mood, poor concentration, and irritability, women with PND also experience guilt about their inability to look after their new baby. In many countries, health visitors screen for PND using the Edinburgh Postnatal Depression Scale, [6] [7] which identifies depressive symptoms but does not include somatic symptoms such as appetite changes, which can be difficult to assess in most women in the postnatal period.

INCIDENCE/ PREVALENCE

A systematic review of studies from 1980 through March 2004 suggests that the point prevalence of major depressive disorder in predominantly high-income countries is about 5% in the first 3 months postpartum. [8] When minor depression is included, it increases to 13%, with a period prevalence rate of 19%. These figures increase further in low-income countries. [9]

AETIOLOGY/ RISK FACTORS

Four systematic reviews have identified the following risk factors for PND: history of any psychopathology (including antenatal depression and/or a history of previous PND), low social support, poor marital relationship, and recent life events. [10] [11] [12] [13] There is also an increased risk of PND among immigrant populations. [14] Studies from India also suggest that spousal disappointment with the sex of the newborn child, particularly if the child is a girl, is associated with the development of PND. [15] [16]

PROGNOSIS

Most episodes of PND resolve spontaneously within 3 to 6 months, [17] but about 30% of affected mothers are still depressed at the child's first birthday. [18] In resource-rich countries, suicide remains a leading cause of maternal deaths in the first year postpartum, although the postpartum suicide rate is lower than the rate in age-matched, non-postpartum women. [19] [20] PND is also associated with negative effects in the infant, including reduced likelihood of secure attachment, [21] deficits in maternal-infant interactions, [22] and impaired cognitive and emotional development of the child, particularly in boys living in areas of socioeconomic deprivation. [23] [24] These associations remain significant even after controlling for subsequent episodes of depression in the mother. However,

there is also evidence to suggest that later effects on the child are related to chronic or recurrent maternal depression, rather than postpartum depression *per se*. [18] Women whose depression persists beyond 6 months postpartum have been found to have fewer positive interactions with their infants than women who were depressed but whose depressive symptoms ended before 6 months, [25] suggesting that the timing of depression is an important factor in determining its effect on the mother-infant relationship.

AIMS OF INTERVENTION

To improve symptoms, quality of life, and mother-infant interaction, with minimal adverse effects on mother and child.

OUTCOMES

Depression scores (e.g. the Edinburgh Postnatal Depression Scale [6] [7]) and other scales used in studies of depression at other times in life (e.g. the Hamilton Depression Rating Scale [26]) (see overview on Depression in adults: drug and other physical treatments), quality of life, mother-infant interaction (rated using questionnaires or observer-rated videos), effect on marital/family relationship (rated using questionnaires), rates of suicide, and **adverse effects**.

METHODS

Search strategy *BMJ Clinical Evidence* search and appraisal date March 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to March 2014, Embase 1980 to March 2014, The Cochrane Database of Systematic Reviews 2014, issue 3 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this overview were systematic reviews and RCTs published in English, at least single-blinded, and containing more than 20 individuals of whom more than 80% were followed up. The minimum length of follow-up required to include studies was 6 weeks. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributors. In consultation with the expert contributors, studies were selected for inclusion and all data relevant to this overview were extracted into the benefits and harms section of the overview. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' section. **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update, we have removed the following previously reported question: What are the effects of non-drug treatments for postnatal depression? **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this overview (see table, p 9). The categorisation of the quality of the evidence (into high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *BMJ Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of drug treatments for postnatal depression?

OPTION SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI) ANTIDEPRESSANTS (FLUOXETINE, PAROXETINE, AND SERTRALINE)

Depression scores

Sertraline compared with placebo We do not know whether sertraline is more effective than placebo at improving symptoms of depression in women diagnosed with postnatal depression (PND) within 3 months of giving birth. However, sertraline may be more effective than placebo at improving symptoms of depression in women diagnosed with PND within 4 weeks of delivery (low-quality evidence).

Sertraline compared with nortriptyline Sertraline may be as effective as nortriptyline at improving depression scores at 8 weeks' follow-up in women meeting DSM-IV criteria for major depression within 3 months of delivery (very low-quality evidence). Note: despite limited evidence in PND, SSRIs are known to be effective in treating depression in the general population and are, therefore, considered likely to be beneficial for the treatment of PND.

For GRADE evaluation of interventions for postnatal depression, see table, p 9 .

Benefits:

SSRIs versus placebo

Fluoxetine versus placebo:

We found two systematic reviews (both with a search date of 2013 [27] [28]). The reviews identified no RCTs comparing fluoxetine with placebo. We found no additional or subsequent RCTs.

Paroxetine versus placebo:

We found two systematic reviews (both with a search date of 2013 [27] [28]) that identified the same single RCT comparing paroxetine with placebo. [29] The RCT does not meet *BMJ Clinical Evidence* reporting criteria (loss to follow-up >20%). However, due to the lack of evidence for postnatal depression, results from the RCT are presented in the Comment section, p 4 .

Sertraline versus placebo:

We found two systematic reviews (both with a search date of 2013 [27] [28]) that identified the same single RCT comparing sertraline with placebo. [30] The RCT (36 women with postnatal depression) compared sertraline with placebo for 6 weeks. [30] The diagnosis of postpartum depression was based on DSM-IV criteria, with a modification to include women with an onset of depression within 3 months of delivery rather than within the 4 weeks stipulated by DSM-IV or DSM-5. All women had depressive symptoms that were rated at least moderate in severity according to the Clinical Global Impression (CGI) Scale and had a score between 18 and 45 on the Hamilton Depression Rating (HAM-D) Scale. The RCT found no significant difference between sertraline and placebo in HAM-D score at 6 weeks' treatment (HAM-D score: 8.8 [baseline of 21.9] with sertraline *v* 13.0 [baseline of 22.3] with placebo, P >0.15). However, in the subgroup of women meeting DSM-IV criteria for postnatal depression (27 women), sertraline was associated with a statistically significant improvement in HAM-D score at 6 weeks' treatment (HAM-D score: 8.0 [baseline of 22.1] with sertraline *v* 15.8 [baseline of 22.9] with placebo, P = 0.01).

Additionally, the RCT found that sertraline significantly increased the proportion of women rated as responders to treatment or as remitters at 6 weeks compared with placebo (responders: 10/17 [59%] with sertraline *v* 5/19 [26%] with placebo, P = 0.05; remitters: 9/17 [53%] with sertraline *v* 4/19 [21%] with placebo, P = 0.05; differences described in study as statistically significant). Responders were defined as having a score of 10 or lower on the HAM-D, at least a 50% decrease in HAM-D score from baseline, and a score of 'much improved' or 'very much improved' on the CGI-Improvement scale. Remitters were defined as those who met the responder criteria and also had a HAM-D score of 7 or lower. For women with an onset of depression within 4 weeks of giving birth (as defined by DSM-IV or DSM-5), the study found that sertraline also significantly increased the proportion of women rated as responders to treatment or as remitters compared with placebo (responders: 6/12 [50%] with sertraline *v* 1/15 [7%] with placebo, P = 0.02; all responders in this group were also remitters).

SSRIs versus antidepressants other than SSRIs

Sertraline versus nortriptyline:

We found two systematic reviews (both with a search date of 2013 [27] [28]) that identified the same single RCT. [31] The RCT (109 women aged 15–45 years meeting DSM-IV criteria for major depression identified within 3 months of delivery, some breastfeeding [proportion not reported]) compared sertraline with nortriptyline. [31] The study found no significant difference in depression severity at 8 weeks between groups, measured using HAM-D, CGI, the Global Assessment Scale (GAS), or the Social Problems Questionnaire (SPQ) (proportion of women with at least 50% reduction in HAM-D score: 31/55 [56%] with sertraline *v* 37/54 [69%] with nortriptyline, P = 0.19).

Harms:

SSRIs versus placebo
Fluoxetine versus placebo:
We found no RCTs.

Paroxetine versus placebo:
We found no RCTs.

Sertraline versus placebo:
Effects on the mother
The RCT noted that three women given sertraline reported adverse effects, which included diarrhoea (1/17 [6%]), headache (1/17 [6%]) and nausea (3/17 [18%]). [30] One person in the placebo group reported developing diarrhoea.

Effects on the infant
There were no adverse events reported for the infants in either group. [30]

SSRIs versus antidepressants other than SSRIs
Sertraline versus nortriptyline:
Effects on the mother
The RCT found no significant difference in the proportion of people who had adverse effects between sertraline and nortriptyline (proportion affected not reported; reported as not significant). [31] People who used nortriptyline most commonly reported thirst, painful dry mouth, and constipation as adverse effects. People who used sertraline most commonly reported headaches, perspiration, and hot flushes. [31]

See Harms of Antidepressants in review on Depression in adults: drug and other physical treatments.

Effects on the infant
The RCT gave no information about harms in the infants. [31] All antidepressants are excreted into breast milk to a greater or lesser extent. [32] A meta-analysis of antidepressant levels in breastfed infants of mothers taking antidepressants found that nortriptyline, paroxetine, and sertraline usually produced undetectable levels in nursing infants. The largest proportion of high antidepressant levels in infants (above 10% of the average maternal level) occurred with fluoxetine (22%) and citalopram (17%). [32] We found a lack of research on long-term risks to the developing child from maternal use of antidepressants.

Comment:

One RCT comparing sertraline with transdermal estradiol or placebo was published after the search date of this overview (August 2015). [33] The results of this study will be assessed for the next update of this overview.

Fluoxetine plus CBT versus CBT alone:
We found three systematic reviews (search dates 2006; [34] [35] and 2004 with two update searches, times not reported [36]), which all identified the same single RCT. [37] The RCT identified by the reviews (87 women recruited by community-based screening, 51 with major depression, 36 with minor depression diagnosed using standardised criteria, [38] breastfeeding women excluded) evaluated four treatments: fluoxetine plus one session of CBT; fluoxetine plus six sessions of CBT; placebo plus one session of CBT; and placebo plus six sessions of CBT. The CBT was delivered by non-specialists after brief training. [37] Significance was assessed together for both fluoxetine groups versus both placebo groups. [39] The RCT found that fluoxetine (plus either 1 or 6 sessions of CBT) significantly improved depression severity scores compared with placebo (plus either 1 or 6 sessions of CBT) at both 4 and 12 weeks (geometric mean difference in Clinical Interview Schedule [CIS]-Revised scores: 4 weeks: 37%, 95% CI 6% to 58%; 12 weeks: 39%, 95% CI 10% to 61%). [37] The RCT gave no information on infant outcomes (see also Benefits of Prescription antidepressant drugs in the overview on Depression in adults: drug and other physical treatments).The RCT gave no information on harms. [37]

Paroxetine versus placebo:
The RCT (70 women with major depressive disorder within 3 months of delivery) compared paroxetine with placebo for 8 weeks. [29] Participants had a score of at least 16 on the 17-item Hamilton Rating Scale for Depression (HRS-D17) at recruitment. The RCT found that, compared with placebo, paroxetine significantly improved depression measured by the CGI-Severity (CGI-S) scale at 8 weeks (difference in mean change in CGI-S over 8 weeks between paroxetine and placebo: –0.48, P = 0.047), but found no significant difference between paroxetine and placebo in the mean change in HRS-D17 (difference between the groups reported as not significant) or Inventory of Depressive Symptomatology Self Report (IDS-SR) scores (difference in mean change over 8 weeks between the groups reported as not significant). Loss to follow-up during the study was high, with 31/70 (44%) completing the trial, meaning that results should be interpreted with caution.

The RCT reported no significant differences between paroxetine and placebo in the proportion of people reporting adverse effects, including decreased appetite, diarrhoea, dizziness, dry mouth, headache, nausea, and somnolence/drowsiness. One participant withdrew from the paroxetine group because of nausea, whereas four participants left the placebo group because of adverse effects (rash, nausea, diarrhoea, and headache).

Sertraline versus nortriptyline:
In the RCT comparing sertraline with nortriptyline, almost half of the eligible participants (97/206) did not sign consent or provide at least 1 week of data. Of the 109 women randomised, 14 were lost to follow-up, withdrew, or did not take the medication for at least 1 week. Significantly more women taking sertraline withdrew from the study in the first 8 weeks compared with nortriptyline (23/55 [42%] with sertraline *v* 13/54 [24%] with nortriptyline; P = 0.03). [31]

Clinical guide
The evidence included in this review is not clearly favourable to SSRIs in the treatment of PND. These findings may be attributable to limitations of the identified evidence, such as heterogeneity in diagnostic criteria and scales used to measure symptomatology, in addition to small sample sizes and possibly insufficient time of follow-up. For example, antidepressant treatment is recommended for at least for 6 months, while the mean treatment time in the study of sertraline versus placebo was only 6 weeks. It is generally assumed that, despite the lack of good-quality evidence comparing SSRIs with placebo directly, SSRIs are likely to be beneficial for the treatment of postnatal depression based on the evidence of their effectiveness in treating depressive disorders in general. However, this generalisation is not free of bias, as pregnancy and postnatal women are a special population with specified characteristics.

OPTION ANTIDEPRESSANTS OTHER THAN SSRIS

Depression scores
Nortriptyline compared with sertraline Nortriptyline may be as effective as sertraline at improving depression scores at 8 weeks' follow-up, in women meeting DSM-IV criteria for major depression within 3 months of delivery (very low-quality evidence). Note: despite limited evidence in postnatal depression, antidepressants other than SSRIs are known to be effective in treating depression in the general population, and are therefore considered likely to be beneficial for the treatment of postnatal depression.

For GRADE evaluation of interventions for postnatal depression, see table, p 9 .

Benefits:

Nortriptyline versus sertraline:
See Benefits of SSRIs, p 4 .

Harms:

Nortriptyline versus sertraline:
See Harms of SSRIs, p 4 . See also option on Antidepressants in the overview on Depression in adults: drug and other physical treatments.

Comment:

See Comment on SSRIs, p 4 .

Clinical guide
Despite limited evidence in postnatal depression, antidepressants other than SSRIs are known to be effective in treating depression in the general population and are, therefore, considered likely to be beneficial for the treatment of postnatal depression.

OPTION HORMONES

Depression score
Oestrogen compared with placebo Oestrogen treatment may be more effective than placebo at improving postnatal depression (PND) at 3 and 6 months in women with severe PND (low-quality evidence). Note: we found no clinically important results about the effects of other hormones in women with PND.

For GRADE evaluation of interventions for postnatal depression, see table, p 9 .

Benefits:

Oestrogen versus placebo:
We found one systematic review (search date 2010 [40]), which identified a single RCT. [41] The RCT (61 women with major depression, 3–18 months postpartum at enrolment, recruited from outpatient clinics, general practitioners, and self-referrals) compared oestrogen treatment (estradiol skin patches for 6 months plus additional dydrogesterone tablets for 12 days each month) with placebo (patches and tablets). [40] Women were excluded if they were breastfeeding, had a medical history that would contraindicate oestrogen treatment, or had changed psychotropic medication in the previous 6 weeks. The RCT found a significantly larger reduction in Edinburgh Postnatal De-

pression Scale (EPDS) scores with oestrogen compared with placebo, both at 3 and 6 months (WMD at 3 months –3.2, 95% CI –6.0 to –0.4; at 6 months –4.4, 95% CI –6.9 to –1.9). [40] The RCT gave no information on infant outcomes.

Other hormone treatments versus placebo:
We found no systematic reviews or RCTs.

Harms:

Oestrogen versus placebo:
Effects on the mother
Endometrial curettage was performed at 6 months on all women in the RCT, and three women who received oestrogen had endometrial changes. [41] These changes had resolved by follow-up at 9 months in all three women. [41] One woman in the oestrogen group, who had been admitted to a psychiatric ward soon after the start of the study because of her worsening mental state, committed suicide. However, her clinical consultant had stopped the oestrogen treatment soon after admission. For harms of oestrogen treatment see also overview on Menopausal symptoms.

Effects on the infant
The RCT gave no information on harms to the infant. [41]

Comment:

Clinical guide
At present there is insufficient evidence available to justify the use of hormone treatment for postnatal depression in routine clinical practice.

One RCT comparing sertraline with transdermal estradiol or placebo was published after the search date of this overview (August 2015). [33] The results of this study will be assessed for the next update of this overview.

OPTION ST JOHN'S WORT (HYPERICUM PERFORATUM)

We found no clinically important results about the effects of St John's Wort in postnatal depression.

For GRADE evaluation of interventions for postnatal depression, **see table, p 9** **.**

Benefits: We found no systematic reviews or RCTs.

Harms: We found no systematic reviews or RCTs.

Comment: One systematic review that reported the results of observational studies found weak evidence that St John's Wort use during lactation did not affect maternal milk production or infant weight. However, in a few cases, it may cause infant colic, drowsiness, or lethargy. Although we found no RCTs evaluating the effects of St John's Wort in postnatal depression, there have been several RCTs of St John's Wort in the treatment of depression outside of the perinatal period. These have been analysed in a systematic review. [42]

GLOSSARY

Clinical Global Impression Scale A one-item, observer-rated scale for measuring the severity of a condition. It has been investigated for validity and reliability. The scale is scored from 0 (not ill at all) to 7 (severely ill).

Clinical Interview Schedule-Revised (CIS-R) A semistructured interview covering non-psychotic symptoms, particularly those associated with depression and anxiety.

Edinburgh Postnatal Depression Scale (EPDS) Designed as a screening questionnaire to identify possible depression in a clinical or research setting. The EPDS has a high sensitivity (95%) and specificity (93%) for postnatal depression, and is used by many health visitors and in many clinical research studies of postnatal depression. The EPDS consists of 10 questions, with responses scored on a 4-point scale according to increased severity of the symptom. Total scores range from 0 to 30 with a score 12 or greater indicating probable depression.

Hamilton Depression Rating Scale (HAM-D) A measure of depressive symptoms using 17 items, with total scores from 0 to 54 (higher scores indicate increased severity of depression).

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Selective serotonin reuptake inhibitor (SSRI) antidepressants (fluoxetine, paroxetine, and sertraline) Two systematic reviews [27] [28] and one RCT [30] added. Categorisation unchanged (likely to be beneficial).

Hormones One systematic review updated. [40] Categorisation unchanged (unknown effectiveness).

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TABLE 1 **Diagnostic criteria for postnatal depression.**

Psychiatric classification	Criteria for postnatal depression
ICD-10, WHO	Depressed mood for most of the day Loss of interest or pleasure in normally pleasurable activities such as playing with the baby Tiredness, decreased energy, and fatigue Additionally, any four of the following should be present: Loss of confidence and self-esteem Feelings of guilt and blaming oneself Recurrent thoughts of suicide or death, including that of the child Difficulty in concentration Agitation or lethargy Sleep disturbance Appetite disturbance
DSM-5 – Perinatal onset specifier	*Onset of depressive episode must be in pregnancy or within 4 weeks postpartum* Symptoms do not differ from symptoms in non-postpartum mood episodes and may include: Fluctuations in mood Preoccupation with infant wellbeing Severe anxiety Panic attacks Fearfulness of being alone with infant

TABLE **GRADE evaluation of interventions for postnatal depression**

Important outcomes			**Depression score, quality of life, suicide, adverse effects**						
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of drug treatments for postnatal depression?									
1 (36) [30]	Depression score	Sertraline *v* placebo	4	–1	0	–1	0	Low	Quality point deducted for sparse data; consistency point deducted for difference in effect in subgroup and for difference in statistical significance of results between dichotomous and continuous outcome measures
1 (109) [31]	Depression score	Sertraline *v* nortriptyline	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and high withdrawal rate; directness point deducted for recruitment issues
1 (61) [41]	Depression score	Oestrogen *v* placebo	4	–1	0	–1	0	Low	Quality point deducted for sparse data; directness point deducted for narrow inclusion criteria

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion. Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.